REMARKS/ARGUMENTS

Claims 1-5, 7-14, and 19-56 are pending.

Claims 1-2, 5, 9, and 12-14 have been amended.

Claims 6 and 15-18 have been cancelled.

Claims 21-56 have been added.

Support for the amendments is found in the claims and specification, as originally filed. Specifically, support for the amendment of claims 1 and 9 can be found at page 18, lines 11-19; support for claims 5 and 12-14 can be found in figures 1, 3; support for claims 19-20 can be found in figures 1, 3 and pages 25-30; support for claim 21 can be found at page 26, second full paragraph; support for claim 22 can be found at pages 25-26 and figure 1; support for claim 23 can be found at pages 8-9, bridging paragraph and page 18, lines 9-10; support for claim 24 can be found at pages 8-9, bridging paragraph and page 18, lines 9-10, and claim 4; support for claim 25 can be found at page 8, lines 3-5, and page 19, lines 23-25; support for claim 26 can be found at pages 33, line 18 to page 34, line 2; support for claim 27 can be found at page 36, Table 1; support for claims 28-29 can be found at pages 16-17, bridging paragraph. New claims 30-56 are similar to claims 1-27, wherein support for the limitation "the ratio in volume between the regeneration region and the denaturation region is about 7:1" can be found at pages 39-40, bridging paragraph.

No new matter is believed to have been added.

Applicants submitted a certified copy of the foreign application JP 2003-273430 on October 1, 2006 to perfect foreign priority. 37 C.F.R. § 1.55(2)-(4). Applicants submit an English translation of the priority application JP 2003-273430, as requested by the Examiner.

Applicants submit a substitute Figure 9 in response to the Examiner objection.

The IDS references cited in the specification, page 4, i.e., JP 06-30776, JP 2003-70490, and Kopp, Science, 1998, were submitted with the IDS filed on January 10, 2006.

The Examiner also crossed out references AO, AP, AQ, AR, AS, and AT listed in the IDS submitted on January 10, 2006, and indicated that these references had not been considered because applicants had not provided English translations.

Applicants submitted English abstracts (i.e., a concise explanation of relevancy) for crossed out references mentioned above with the IDS, and, therefore, have met the requirement of 37 C.F.R. § 1.98. Applicants kindly request the consideration of the crossed out references and forward the initialed copy of the IDS with the next Official Action.

Claim Rejections.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph because the Examiner believes that the arrangement of the flow channel is not clear. Amended claim 5 clearly recites that the denaturation region is followed by the regeneration region. Applicants request that the rejection be withdrawn.

Claims 1-5, 7-14, and 19-27 are directed to an amplifier and a method for amplification of a nucleic acid in a flow channel comprising a denaturation and regeneration region, wherein a nucleic acid synthetase is immobilized in the regeneration region and has an optimum temperature of 30-40 °C. Claims 28-29 are directed to an amplifier and a method for amplification comprising a denaturation and regeneration region, wherein regeneration region has an optimum temperature of 30-40 °C. Using a low optimal temperature synthetase is advantageous because enzymes that have hardly been used together in the conventional PCR. The cited prior art references do not describe DNA amplification that can be accomplished by a synthetase having an optimum temperature of 30-40 °C.

Claims 30-56 are directed to an amplifier and a method for amplification comprising a denaturation and regeneration region, wherein the ratio in volume between the regeneration region and the denaturation region about 7:1. Claims 35 and 44-47 in addition claim a synthetase having an optimum temperature of 30-40 °C. The cited prior art references do not describe the ratio in volume between the regeneration region and the denaturation region being about 7:1. This condition allows regulating denaturing/annealing/extension time of the PCR

Claims 1-2, 4-5, 7, 9, 11-12, 14, and 19 are rejected under 35 U.S.C. 102(b) over Misako, JP 2003-174900.

The amplifier and the method of amplifying a nucleic acid template of claims 1-5, 7-14, and 19-29 comprise using a nucleic acid synthetase having an optimum temperature of 30 to 40°C.

The amplifier and the method of claims 30-56 requires the ratio in volume between the regeneration region and the denaturation region to be about 7:1.

Misako describes a circulating amplification process and an amplifier having a flow channel. However, Misako describes using "heating at high temperature section 5" (fig. 3), i.e., a usual PCR process utilizing a thermostable polymerase. Misako does not disclose that polymerization is conducted by an unusual high temperature sensitive enzyme having a low optimum temperature, i.e., at 30-40 °C (see claims 1-5, 7-14, and 19-27). Misako also does not teach a regeneration region having an optimum temperature of 30 to 40 °C (see claims 28-29). Using a low optimal temperature synthetase is advantageous because enzymes that have hardly been used together in the conventional PCR (e.g., described by Misako), can be used together to improve reliability of the amplification (see this specification at pages 8-9, bridging paragraph).

Misako also does not describe an amplifier having the ratio in volume between the regeneration region and the denaturation region about 7:1 (see claims 30-56). This specification describes that the ratio of the regions is important for regulating denaturing/annealing/extension time of the PCR (page 39-40). Thus, Misako does not anticipate the claimed invention. Applicants request that the rejection be withdrawn.

Claims 3, 10, 13, and 20 are rejected under 35 U.S.C. 102(b) over Misako, JP 2003-174900 and Moses, Mol. Cell. Biol., 14(4):2767-2776 (1994).

Misako does not teach that that polymerization is conducted by an unusual high temperature sensitive enzyme having a low optimum temperature, i.e., at 30-40 °C (see claims 1-5, 7-14, and 19-27). Misako also does not teach that the ratio in volume between the regeneration region and the denaturation region is about 7:1 (see claims 30-56). Moses does not cure this deficiency.

Moses teaches that a DNA polymerase bound to an affinity column is active (e.g., fig. 2 and page 2768, right col.). However, Moses does not disclose using a low temperature synthetase for amplification and an amplifier having the ratio in volume between the regeneration region and the denaturation region is about 7:1. Also none of the references teach a regeneration region having an optimum temperature of 30 to 40 °C (see claims 28-29).

Thus, Misako and Moses do not make the claimed invention obvious. Applicants request that the rejection be withdrawn.

Claims 5, 12, and 14 are rejected under 35 U.S.C. 102(b) over Misako, JP 2003-174900 and Hideo, JP 6-30776.

Misako does not teach that that polymerization is conducted by an unusual high temperature sensitive enzyme having a low optimum temperature, i.e., at 30-40 °C (see claims 1-5, 7-14, and 19-27). Misako also does not teach that the ratio in volume between the

regeneration region and the denaturation region is about 7:1 (see claims 30-56). Hideo does not cure this deficiency.

Hideo teaches carrying an amplification reaction by transporting a reaction solution as a mobile phase through various reaction sections (fig. 1-2, abstract). However, Hideo does not disclose using a low temperature synthetase for amplification and an amplifier having the ratio in volume between the regeneration region and the denaturation region is about 7:1 (see claims 30-56).

Also none of the references teache a regeneration region having an optimum temperature of 30 to 40 °C (see claim 28-29). Thus, Misako and Hideo do not make the claimed invention obvious. Applicants request that the rejection be withdrawn.

Claim 13 is rejected under 35 U.S.C. 102(b) over Misako, JP 2003-174900, in view of Moses, Mol. Cell. Biol., 14(4):2767-2776 (1994), and Hideo, JP 6-30776.

The teachings of Misako, Moses, and Hideo are set forth above. None of the references teach using a low temperature synthetase for amplification (see claims 1-5, 7-14, and 19-27) and an amplifier having the ratio in volume between the regeneration region and the denaturation region is about 7:1 (see claims 30-56). Also none of the references teach a regeneration region having an optimum temperature of 30 to 40°C (see claims 28-29). Thus, the combination of the Misako, Moses, and Hideo references do not make the claimed invention obvious. Applicants request that the rejection be withdrawn.

Claims 6, 15, 17, and 18 are rejected under 35 U.S.C. 102(b) over Misako, JP 2003-174900, and Schleper, J. Bacteriol., 179(24):7803-7811 (1997).

Misako does not describe a device having the polymerase-immobilized region that would be optimum for the enzyme described in Schleper. There is also no disclosure in Schleper that amplification of DNA can be accomplished reliably with the *Cenarchaeum symbiosum* polymerase. Schleper only discloses that *C. symbiosum* DNA polymerase exhibit

its highest specific activity with gapped-duplex DNA as a substrate (abstract, fig. 4), but does not teach using the isolated enzyme for DNA amplification reaction such as disclosed in Misako. Also an optimum temperature of the polymerization activity on the gapped-duplex DNA of the Schleper enzyme is 42°C, while its 3'-5'-exonuclease activity temperature is 38 °C (fig. 4, and page 7807, right col) (see claims 1-5, 7-14, and 19-27). Therefore, in terms of the nucleic acid synthetase, there is no motivation of using the enzyme having optimum temperature rage as claimed, arising neither from Misako nor from Schleper, in the claimed amplifier and amplification method. One would not have been motivated by Schleper to modify the device of Misako.

None of the references teach using a low temperature synthetase for amplification (see claims 1-5, 7-14, and 19-27), an amplifier having the ratio in volume between the regeneration region and the denaturation region is about 7:1 (see claims 30-56), and a regeneration region having an optimum temperature of 30 to 40 °C (see claims 28-29). Thus, Misako and Schleper do not make the claimed invention obvious. Applicants request that the rejection be withdrawn.

Claim 8 is rejected under 35 U.S.C. 102(b) over Misako, JP 2003-174900, and Southgate, US 5,863,801.

Misako does not teach that that polymerization is conducted by an unusual high temperature sensitive enzyme having a low optimum temperature, i.e., at 30-40 °C (see claims 1-5, 7-14, and 19-27). Misako also does not teach that the ratio in volume between the regeneration region and the denaturation region is about 7:1 (see claims 28-29). Southgate does not cure this deficiency.

Southgate describes a device and a method for automatic isolation of a nucleic acid comprising pumps that can reverse the flow of reagents (col. 20, lines 11-25). However, Southgate does not disclose using a low temperature synthetase for amplification (see claims

1-5, 7-14, and 19-27) and an amplifier having the ratio in volume between the regeneration region and the denaturation region is about 7:1 (see claims 30-56). Also neither Misako nor Southgate teaches a regeneration region having an optimum temperature of 30 to 40 °C (see claims 28-29). Thus, Misako and Southgate do not make the claimed invention obvious. Applicants request that the rejection be withdrawn.

A Notice of Allowance for all pending claims is requested.

Respectfully submitted,

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